CLAIMS

What is claimed is:

1. A tandem mass spectrometer comprising sequentially connected pulsed ion source, a parent ion separator, a fragmentation cell, a second time-of-flight mass spectrometer (TOF2) and a time nested data acquisition system, acquiring fragment mass spectra for multiple parent ions, wherein to improve resolution of parent ion separation the said parent ion separator is a time-of-flight mass spectrometer and wherein, for ions of the same mass-to-charge ratio, time-of-flight in the said TOF1 is significantly larger than both passage time through the said fragmentation cell and time-of-light in the said TOF2.

2. A tandem mass spectrometer of claim 1, wherein time-of-flight in the said TOF1 is at least 10 times larger than time-of-flight in the said TOF2.

3. A tandem mass spectrometer of claim 1, wherein average ion energy in the said TOF1 is at least 100 times smaller than in the said TOF2.

4. The tandem mass spectrometer of claim 1, wherein the pulsed ion source is MALDI ion source with gas pressure from vacuum up to 0.1mbar.

5. The tandem mass spectrometer of claim 1, wherein the pulsed ion source comprises a pulse operating radio frequency (RF) storage device and a continuous ion source of the following list: an Electrospray source, a MALDI ion source, filled with gas at gas pressure between 10mtorr and 1atm, an electron impact ion source, electron impact with chemical ionization ion source, or photo ionization ion source; ions are continuously supplies from any of said ion sources to become accumulated and pulse-ejected out of the said storage device.

6. The tandem mass spectrometer of claim 5, wherein said storage device comprises at least one RF-only linear multipole, supplemented by at least one DC electrode, creating non-zero axial electric field.

7. The tandem mass spectrometer of claim1, wherein said TOF1 comprises RF only linear multipole, surrounded by two pulsed mirrors with axial quadratic electric field.

8. The tandem mass spectrometer of claim1, wherein said TOF1 comprises two dimensional RF-only ion tunnel, surrounded by two-dimensional DC mirrors with quadratic electric field.

9. The tandem mass spectrometer of claim 1, wherein said TOF1 comprises at least a pair of coaxial electrodes with DC voltage applied between them and wherein ions are injected between said electrodes at an angle to their axis.

10. The tandem mass spectrometer of claim 9, wherein ions enter and exit the gap between said electrodes through a cut-off boundaries, which are formed by double sided printed circuit boards

11. The tandem mass spectrometer of claim 1, wherein said TOF1 is a planar multi-pass electrostatic TOF, comprising a two-dimensional free flight channel and two planar focusing electrostatic mirrors, composed of focusing and reflecting electrodes.

12. The tandem mass spectrometer of claim 1, wherein said TOF1 is a cylindrical multi-pass electrostatic TOF, comprising at least a pair of coaxial cylinders with radial deflection and two focusing electrostatic mirrors, composed of coaxial cylinders.

13. The tandem mass spectrometer of claim 1, comprising an additional timed gate between said TOF1 and said fragmentation cell, which is capable of transmitting ions only within multiple narrow time windows.

14. The tandem mass spectrometer of claim 1, wherein energy of ion injection into said fragmentation cell is adjusted by the electrostatic offset between said TOF1 and said fragmentation cell. The offset may be adjusted during TOF1 separation to provide mass dependent ion energy around 50V/kD, optimum for parent fragmentation.

15. The tandem mass spectrometer of claim 1, wherein said fragmentation cell is collision induced dissociation (CID) cell, filled with gas and comprising at least one RF-only multipole, supplemented by at least one DC electrode.

16. The tandem mass spectrometer of claim 13, wherein the time spread of ion packet within said CID cell is reduced by using short cell of less than 1cm long, high gas pressure above 100mtorr.

17. The tandem mass spectrometer of claim 13, wherein for the purposes of time compression, the collision cell stores fragment ions using modulation of axial DC field within the cell, and ejects pulsed beam synchronized with TOF2 pulses.

18. The tandem mass spectrometer of claim1, wherein said fragmentation cell comprises a pulsed temporal and spatial focusing lens and a target, coated by fluoro-hydrocarbon monolayer.

19. The tandem mass spectrometer of claim 1, wherein the TOF2 is a TOF MS with an orthogonal time injection (o-TOF MS).

20. The tandem mass spectrometer of claim 1, wherein said TOF2 comprises a high current detector and transient recorder.

21. The tandem mass spectrometer of claim 1, wherein resolution of time separation in the TOF1 is enhanced by any of the following means: any reflector of the TOF1 forms quadratic potential distribution along ion path, using large number of reflections in the TOF1, using TOF1 longer than 1m, using said timed gate with multiple narrow time windows.

22. The tandem mass spectrometer of claim 1, wherein an additional in-line detector is installed anywhere after TOF1.

23. Method of comprehensive MS-MS analysis, comprising the following steps:

24. pulse ejection of plurality of parent ions with various mass-to-charge ratio (M/Z) out of a pulsed ion source;

25. time separation of parent ions within a first time separator;

26. fragmentation of time-separated ions;

27. mass analysis of fragment ions within a second time-of-flight mass spectrometer (TOF2);

28. Time nested fragment mass spectra acquisition corresponding to multiple parent ions per every single ion pulse without mixing fragment spectra of different parent ions,

29. wherein for the purpose of improving sensitivity and throughput of MS-MS analysis, said time separation occurs within a time-of-flight mass spectrometer (TOF1) and wherein time of said parent ion separation significantly exceeds time of both said fragmentation and said fragment mass analysis.

30. The method of comprehensive MS-MS analysis, wherein said time of flight in the said TOF1 is at least 10 times larger than in the said TOF2.

31. The method of MS-MS analysis of claim 23, wherein the ion pulse is generated in a MALDI ion source with gas pressure from vacuum up to 100mTorr.

32. The method of MS-MS analysis of claim 23, wherein said ion pulse is formed by pulsed ejection out of storage quadrupole, while ions are introduced into the storage quadrupole out a continuous ion source of the following list: an Electrospray source, a MALDI ion source, filled with gas at gas pressure between 10mtorr and 1atm, an electron impact ion source, electron impact with chemical ionization ion source, or photo ionization ion source.

33. The method of MS-MS analysis of claim 23, wherein said time separation of parent ions occurs in quadratic DC field and wherein energy of ions in said TOF1 is at least 100 times less than in said TOF2.

34. The method of MS-MS analysis of claim 26, wherein said time separation of parent ions in quadratic DC field is achieved with assistance of confining radio-frequency field in at least one dimension, orthogonal to DC field.

35. The method of MS-MS analysis of claim 27, wherein said ion confinement in RF only field is achieved along one axis, ions are injected from one end of the RF field zone and after multiple reflections in pulsed quadratic DC field are released on the other end.

36. The method of MS-MS analysis of claim 27, wherein the parent ion confinement by RF-only field is achieved along two dimensional plane. Ions are injected at small angle to TOF1 axis, which is parallel to gradient of DC field. Ions experience multiple reflections in DC field, while slowly drifting in orthogonal direction, towards the exit of RF-filed.

37. The method of MS-MS analysis of claim 23, wherein said time separation of parent ions occurs in electrostatic field and wherein the said energy of ions in the first time-of-flight separator is at least 10 times smaller than in the said second time-of-flight mass spectrometer, and wherein the said effective flight path in the said first time-of-flight separator is at least 30 times larger than in the said second time-of-flight mass spectrometer.

38. The method of MS-MS analysis of claim 23, wherein said time separation of parent ions occurs in electrostatic field, created by a pair of coaxial electrodes, and wherein ions are injected into said electrostatic field at an angle to electrode axis, and wherein disturbance of said electrostatic field at boundaries is reduced by double sided printed circuit boards.

39. The method of MS-MS analysis of claim 23, wherein said time separation of parent ions occurs in planar electrostatic field, formed by planar free flight channel and planar focusing griddles ion mirrors. Ions are injected at small angle to TOF1 axis and experience multiple bounces between mirrors.

40. The method of MS-MS analysis of claim 23, wherein said time separation of parent ions occurs in cylindrical electrostatic field, formed by multiple pairs of coaxial cylinders. In at least one pair radial field is applied. The cylindrical field

between cylinders is analogous to field of claim 32. Ions are injected at small angle to TOF1 axis and experience multiple bounces between mirrors.

41. The method of MS-MS analysis of claim 23, wherein resolution of time separation in TOF1 is enhanced by sampling multiple narrow time windows before submitting ions to said fragmentation step.

42. The method of MS-MS analysis of claim 23, where said fragmentation is achieved in one of the following processes: in energetic collisions with gas, in collision with surface, by light.

43. The method of MS-MS analysis of claim 23, wherein the analysis is made in two steps: step 1 of acquiring parent mass spectrum in TOF2, while using TOF1 in a pass mode, and step 2 of sampling narrow time windows in front of collision cell, corresponding to arrival of meaningful parent ions and acquiring fragment spectra for those time windows only. Said time windows are selected on the fly, based on parent masses out of stage 1 measurements.

44. The method of MS-MS analysis of claim 23, wherein a "parent scan", i.e. spectrum of parent ions having a predetermined set of fragment ions, is reconstructed out of a full MS/MS data set.

45. Method of LC-MS-MS analysis or LC-LC-MS-MS analysis, wherein the flow of solvent is continuously introduced out of LC into a tandem mass spectrometer of claim 1 and MS-MS data are acquired using method, described in claims 21 to 37.